Recent Publications
Babies act purposefully – Serene aging – Flexible connections – Sense of orientation – Neurons in unison

Meet the scientist
Ad Aertsen

News and Events
Personalia – New Bernstein Facility established – Simulation App developed – ECVP in Bremen – Book about honeybees – Bernstein TV – Bernstein in social networks
Babies can act on purpose early on

Infants can act purposefully much earlier than developmental psychologists previously believed: At the age of six months, the brains of infants are sufficiently developed that they are able to perform targeted actions through eye movements. This study was performed by a research team from the Bernstein Focus Neurotechnology Frankfurt, the Frankfurt Institute for Advanced Studies and the Goethe University Frankfurt.

Utilizing eye-trackers, the researchers measured the eye movements of infants, which the infants were using to control a computer. After they directly looked at a red dot on the screen, with a delay of 0.6 seconds, a tone and an alternating animal picture was presented. Six to eight-month-old infants learned very quickly to summon the animal picture by gazing on the red “button”. And they could not get enough: Within a minute, the six-month-old infants summoned the image with their eyes about 15 times.

This research provides new insights into early childhood brain development. Up until now, deliberate infant actions were recorded by other movements, such as pointing or pressing a switch. The fine motor skills of the arms and legs, however, develop only at the age of eight to ten months to the extent that the children can perform such movements. Therefore, up to now investigations were not possible at earlier ages.

The research team led by cognitive scientist Jochen Triesch and the developmental psychologist Monika Knopf has used devices for measuring the eye movements (eye-tracker) of the infants, since children are able to precisely control eye movements from the age of about four months. The experiments have shown that the children use these options intentionally: After just a few trials, the children looked at the position of the screen where the new animal picture was expected to appear before it was actually there. Even on a screen with two identical-looking red buttons they soon found out which one makes the animal picture appear and looked specifically towards it – it seems as if they understood this relationship even faster and more accurately than a control group of adult subjects that performed the same test.

Eye tracking enables researchers to study the targeted actions of infants before the development of fine motor skills and language. “With this method, the child’s development can be investigated earlier than before,” explains Triesch, who sees prospects for further work on brain development: “Among other things, we want to know if this method is suitable for even younger babies.”

Serenity in older age

Older people can deal with missed opportunities more easily than the young, according to researchers at the University Medical Center Hamburg-Eppendorf and the Bernstein Focus Neuronal Basis of Learning (Project: Complex Human Learning. One reason might be found in a brain region that is important for the link between emotion and control. Its activity is increased in healthy older people when they are confronted with a missed opportunity. This is not the case in young people and people with late-life depression, who can be influenced significantly by missed chances. “The findings could aid the development of behavioral treatments for depression in the elderly,” explains the principal investigator Stefanie Brassen.

“If I’d only...”. Why do older people often react in a more relaxed fashion when faced with missed opportunities and wrong decisions? Motivational lifespan theories explain as follows: The older you are, the less time and fewer opportunities remain to make up for lost chances. Thus, there is more impetus to cope with the situation, rather than regretting the past. Whether or not there is a neurobiological basis for this adaptive behavior is now being examined by a team around the neuroscientists Stefanie Brassen and Christian Büchel within a project funded by the German Science Foundation (DFG).

Using imaging methods (fMRI), the researchers examined brain activity of healthy young and elderly subjects and of patients with late-life depression while they were playing a simple computer gambling game. The test subjects could gain money or lose recently gained profit. Subsequent to each gain trial, they were shown how much more they could have won, had they taken another decision. How strongly this knowledge influenced their future behavior served as a measure of regret. If the behavior did not change, it was assumed that the decision was not regretted. However, if the test subjects significantly increased or decreased their gambling risk, the researchers accounted this as an indicator for regretting a decision.

Only the healthy elderly subjects did not show signs of regret in response to missed chances, neither in behavior and body functions such as heart beat or sweating, nor in the brain's reward system. Instead, they responded to missed opportunities with a signal increase in a region in the forebrain, the anterior cingulate cortex (ACC). “This ACC activation can be best interpreted as ‘healthy’ counter-regulation,” says Brassen. “Not to regret missed opportunities seems to be an important factor for emotional health in age. Here, the investigated region of the brain plays a key role,” explains Brassen. Future therapies for late-life depression and prevention measures might build on these findings.

Highly flexible despite hard-wiring

One cup or two faces? What we believe to see in one of the most famous optical illusions changes in a split second; and so does the path that the information takes in the brain. In a new theoretical study, scientists of the Max Planck Institute for Dynamics and Self-Organization, the Bernstein Center Göttingen and the German Primate Center now show how this is possible without changing the cellular links of the network. The direction of information flow changes, depending on the time pattern of communication between brain areas. This re-organization can be triggered even by a slight stimulus, such as a scent or sound, at the right time.

The way how the different regions of the brain are connected with each other plays a significant role in information processing. This processing can be changed by assembly and disassembly of neuronal connections between brain areas. But such events are much too slow to explain rapid changes in perception. From experimental studies, it was known that the responsible actions must be at least two orders of magnitude faster. The Göttingen scientists now show for the first time that it is possible to change the information flow in a tightly interconnected network in a simple manner.

Many areas of the brain display rhythmic nerve cell activity. “The interacting brain areas are like metronomes that tick at the same speed and in a distinct temporal pattern,” says the physicist and principal investigator Demian Battaglia. The researchers were now able to demonstrate that this temporal pattern determines information flow. “If one of the metronomes is affected, e.g., through an external stimulus, then it changes beat, ticking in an altered temporal pattern compared to the others. The other areas adapt to this new situation through self-organization, and start playing a different drum beat as well. It is therefore sufficient to impact one of the areas in the network to completely reorganize its functioning, as we have shown in our model,” explains Battaglia.

The applied perturbation does not have to be particularly strong. “It is more important that the ‘kick’ occurs at exactly the right time of the rhythm,” says Battaglia. This might play a significant role for perception processes: “When viewing a picture, we are trained to recognize faces as quickly as possible—even if there aren’t any,” points out the Göttingen researcher. “But if we smell a fragrance reminiscent of wine, we immediately see the cup in the picture. This allows us to quickly adjust to things that we did not expect by changing the focus of our attention.”

Next, the scientists want to test the model on networks with a more realistic anatomy. They also hope that the findings will inspire future experimental studies, as Battaglia says: “It would be fantastic if, in some years, certain brain areas could be stimulated in such a subtle and precise manner that the theoretically predicted effects can be measured by imaging methods.”

To the beat of grid cells

To learn how we human beings find our way in the world, neurobiologists have long used rats and mice as model systems. Recently, “grid cells” have been discovered in rodents, that are active when the animal navigates through certain areas of its environment. A grid cell fires whenever the rat or mouse is at a node of an imaginary hexagonal grid, overlaid on the topography of the outside world. In the past, one commonly assumed that the brain computes the animal’s spatial location from the time-course of the grid cells’ average neural activity, as the timing of individual nerve impulses was believed to be too imprecise. However, researchers at the Bernstein Centers Berlin and Munich, Humboldt-Universität zu Berlin and Ludwig-Maximilians-Universität München have now shown the opposite to be true: by taking the time sequence of nerve impulses into consideration, one can determine the animal’s position with twice the accuracy than by the number of impulses alone. The timing pattern is clearly evident already in the grid cell’s activity during a single run. “The animal can, therefore, use the precise temporal information to guide its behavior,” says neuroscientist Andreas Herz, who directed the study.

The discovery of grid cells in the laboratory of Edvard Moser (Trondheim) in 2004 has captivated many scientists. Not only do average activity patterns of these cells regularly repeat across space, producing hexagonal grids in the spatial map of firing rates, but their temporal patterns of firing are also elaborate. The rhythmic activity on a coarse scale, as measured by the local EEG (electroencephalogram), organizes and defines the fine temporal structure of the firing in single grid cells: as the animal approaches one of the imaginary nodes of the hexagonal lattice, the cell first becomes active only during the late phase of the EEG oscillation. As the animal continues to move, the nerve impulses shift in time to ever earlier phases.

Until now, this phenomenon was only observed after averaging the data over many runs of the animal, which allowed doubts regarding its biological relevance. The new analysis reveals that the temporal shift in a grid cell’s impulses is not only present on single runs, but the shift is even more pronounced than in data pooled over many runs. The results support the view that many brain areas rely on the fine temporal activity pattern of nerve cells and less on the amount of activity. Even if the average activity is maintained at a constant level, neurons can use the dimension of time to encode many different signals and improve the brain’s capacity to process information.

In the course of this study, the researchers re-analyzed data from previous experimental studies from the group of Edvard Moser. The data from this group are freely available on the Internet, which made further animal experiments unnecessary.

Neurons in unison

Neurons in local networks often show small correlations between the temporal pattern of their signals, as scientists have often observed in experimental studies. Such observations have been made in many different areas of the brain’s cortex. Intuitively, this is not surprising: Each neuron is connected to thousands of neighbors and reacts to their inputs, which leads us to expect correlations in their activity to occur. However, what remained unclear up until now was whether these correlations bear a significance for the function of the network as a processor of information, and to what extent; or whether they are simply a natural consequence of the dense synaptic wiring. A completely satisfying answer to this question is yet unknown.

Theoretical models have shown how the interplay of the activity of excitatory and inhibitory neurons keeps correlations small. This is an important prerequisite for the brain to fulfill its many tasks. Strong correlations—which could occur when inhibitory neurons do not balance the activity of their excitatory counterparts—would result in a situation of synchronous activation of many nerve cells in which no meaningful processing would be possible any more. This is the case, for example, during an epileptic seizure. However, it has been difficult so far to understand how exactly the detailed pattern of connections between neurons affects or counteracts correlations between specific pairs of neurons.

Volker Pernice and colleagues from the Bernstein Center Freiburg have shown in a recent study how correlations can be traced back to synaptic connections (Pernice et al., *PLoS Comput Biol*, 2011). Their new publication characterizes correlations in networks of “leaky integrate-and-fire neurons”—a widely used simplified model of neurons. Mathematically, the networks were approximated as a linear system—a technique that can describe many nonlinear systems for a limited operating regime with high fidelity.

This theory has for the first time enabled the scientists to understand the influence of different connectivity patterns on the collective dynamics of the neurons even in models of larger networks. The model could be used to better assess the origin of correlations that are observed in local networks: Whether these are natural side effects resulting from the network structure, or whether the strength of the correlations allows the assumption of further interactions with the input signal.

Text: Volker Pernice and Gunnar Grah, Bernstein Center Freiburg


*Predictions from the model (black curves) correspond very well to the actual correlations that were found in the computer simulation of a neural network (red area).*
Ad Aertsen

As a young physics student at Utrecht, Ad Aertsen was not particularly thrilled by the “classical” areas of his field. So he started roaming adjacent fields such as philosophy of science and biophysics. Probably thanks to the fact that much of the neurophysiological research in Holland was conducted in physics departments, he finally found his favorite research subject in the brain. This topic offered plenty of open and exciting questions to which he could apply the tools of physics and math.

During his doctoral studies with Peter Johannesma in Nijmegen, Aertsen began to study hearing in cats and frogs. The researchers followed an approach that actually nowadays still appears quite up-to-date: they sought to relate the response properties of neurons in the auditory system to the animals’ natural environment—their “acoustic biotope”. Already in those early days they applied complex and natural stimuli, next to conventional technical stimuli like pure tones and noise. This allowed them to study how the brain translates properties of environmental stimuli into neuronal activity, i.e., how stimuli are “encoded” in the brain. On the other hand, it also offered the opportunity to “decode” the neural activity, i.e., to reconstruct the sensory environment from the neuronal activity.

Ad Aertsen found out that the response properties of neurons (their “receptive fields”) were not static but dynamic, i.e., they could change with time and with stimulus conditions. The nerve cells apparently did not just linearly add up the incoming stimuli. Rather, there had to be stimulus-dependent, non-linear effects, most likely originating from interactions between nerve cells in the neural network. This insight made clear that, to understand brain function, one could not limit oneself to studying single nerve cells, but rather had to study many neurons simultaneously.

But that strategy brought new problems. Instead of trains of action potentials (‘spikes’) of individual nerve cells, the researchers now had to deal with a whole mess of multiple, simultaneous neuronal spike sequences. With his colleague Michael Erb, Aertsen invented a “device” to make this problem accessible to the senses: Their “neurophone” (a present for the 60th birthday of Valentino Braitenberg) translated the spikes of different neurons to tones of different pitch, such that one could listen to a whole choir of neurons and, maybe, might identify repeating patterns of brain activity as recurring melodies.

As a subjective experience, that was all quite nice, but how would it be possible to evaluate and quantify these patterns more objectively? To this end, as a postdoc with George Gerstein, Philadelphia, USA, Aertsen started to develop appropriate data analysis methods such as the “joint-PSTH” and “gravitational clustering”. These methods could not only deal with the activity of individual neurons, but also assessed the behavior of whole groups of neurons and neuronal interactions, and by that made a whole new dimension of the nervous system accessible.

Simulations of neuronal networks proved to be an enormously helpful tool for testing and calibrating these methods. By simulating networks with known connectivity and subjecting the simulated activity to the analysis tools, one could efficiently check whether and under what conditions the methods arrived at the correct conclusions regarding network structure and interactions.

Neural network simulations have a further advantage: they can be used as an “electronic playground” to systematically
Decoding of grasping movements for motor neuroprostheses: The grasp depicted in blue entails a clearly different brain activity than the one depicted in red.

vary the structure of a network and observe the effects on network activity and dynamics. This made it possible to design computer experiments to address fundamental questions in neurophysiology such as: How does the propagation of neuronal signals depend on network structure? What can one learn from this about the function of these networks and the neural codes presumably entailed therein? Can the functions of different brain areas be deduced from differences in their structure? What impact do activity dependent learning mechanisms have on the development of neural networks and their functions?

In spite of all his enthusiasm for realistic detail, though, Aertsen reminds us that researchers must not forget one basic principle. “Models and simulations must be as simple as possible and only as complex as necessary, not the other way around”. Otherwise, one runs the risk of creating monstrosities like Salman Rushdie described them in his book “Haroun and the Seas of Stories” as “M2C2D for P2C2E: machines too complicated to describe for processes too complicated to explain”. That would not get us any further in our quest for understanding brain function.

Research has shown that “slim” simulations incorporating the key biological principles can not only be used for investigating the healthy brain, but may also provide hints regarding the causes of and even possible therapies for neurological diseases. Once you figured out which critical characteristics of a network give rise to pathological changes in brain activity, one can test in the same simulations which possible interventions could guide the activity back into the normal regime—precisely what Arvind Kumar, Ad Aertsen and colleagues are now trying for the basal ganglia in Parkinson’s disease.

Aertsen and his group also achieved major progress in applying their data analysis methods towards medical application. They recognized early on that the questions on encoding and decoding of brain activity they started asking decades ago opened up exciting new medical options. If one is good enough at decoding environmental stimuli, or, in the case of the motor system, intended movements from neuronal activity, one should also be able to develop neural prostheses that can replace lost body functions by reading out brain activity. That is also why Aertsen participates in the Freiburg Brain-Machine Interface Initiative that investigates how motor neuroprostheses may provide paralyzed people with some motor abilities. Although still under development, such systems are already being tested in first clinical trials in various locations worldwide and could, in the future, significantly increase the quality of life of many patients.

Twenty years ago, no one would have predicted that the seemingly academic question for the neural code would in a relatively short time give rise to such concrete perspectives for medical applications—a perfect example of how basic science keeps opening up new vistas that turn out to be of immense practical use for our daily lives.
Personalia

**Niels Birbaumer** (BFNT Freiburg-Tübingen, University of Tübingen) was awarded on January 27, 2012, the honorary doctorate of Complutense University, Madrid, Spain, for his pioneering work in the development of Brain Computer Interface systems for clinical applications.
www.bcf.uni-freiburg.de/news/awards/20120130-birbaumer

www.nncn.de/nachrichten-en/leiboldcallforpapers

**Alexander Borst** (BCCN Munich, BCOL Network Simulation, MPI of Neurobiology, Martinsried) was elected member of the Bavarian Academy of Sciences. The Bavarian Academy of Sciences was founded in 1759 and is one of the oldest and largest science academies in Germany.
www.neuro.mpg.de/101027/1203_BorstBAW

**Eberhard Zrenner** (BCCN and University Hospital Tübingen) was awarded the honorary doctorate of the Naresuan University for his commitment to the advancement of ophthalmology at this state-run Thai University. The honorary doctorate was presented by princess HRH Maha Chakri Sirindhorn of Thailand on December 19, 2011.
www.medizin.uni-tuebingen.de/Presse_Aktuell/Pressemeldungen/2012_01_13.html (in German)

**Dario Farina** (BFNT and University of Göttingen) receives for the project DEMOVE 2.4 Mio. € over the next five years from the European Research Council (ERC). With DEMOVE, Farina wants to establish a basis for directly connecting computer-controlled prostheses to the nervous system.
http://idw-online.de/de/news469116 (in German)

**Michael Frotscher** (Bernstein Center Freiburg, University Medical Center Hamburg-Eppendorf) was elected Fellow in the section neuroscience of the American Association for the Advancement of Science (AAAS). The AAAS is a non-profit organization dedicated to advancing science, engineering, and innovation throughout the world for the benefit of all people. AAAS is also publisher of the scientific journal “Science”.

© Images: A. Borst: Graduate School of Systemic Neurosciences – Ludwig-Maximilians-Universität München (GSN-LMU); M. Frotscher: Gunnar Grah, Bernstein Center Freiburg; C. Leibold: GSN-LMU; E. Zrenner: University Hospital Tübingen
New Bernstein Facility  
Simulation and Database Technology

In November 2011, the Helmholtz Society decided to establish a “Simulation Laboratory Neuroscience” at Research Center Jülich. Its purpose is to act as an interface between the Jülich Supercomputing Centre (JSC) and the neuroscience community, and to foster the usage of the Jülich computing resources in neuroscience. Starting 2013, the new facility will be funded by the Helmholtz Society.

Since supercomputers work differently than regular computers, neuroscientists will need to adapt the simulations of brain processes to their specific needs and possibilities in order to make optimal use of the Jülich computer power. The Simulation Laboratory Neuroscience offers researchers the opportunity to adapt and optimize their programs together with experts on computational neuroscience, data analysis, anatomy, virtual reality and supercomputing. In addition, the facility will advance the further development and standardization of theoretical models in the field of brain research.

Within the framework of the “Simulation Laboratory Neuroscience”, a “Bernstein Facility Simulation and Database Technology” will be established. Upon proposal by the Research Center Jülich and decision of the Bernstein Project Committee, the new facility will be integrated into the Bernstein Network. The facility offers the network expertise, assistance and consulting services in developing software for supercomputing, integrating new data into large-scale models and in applying for computing times at Research Center Jülich.

http://idw-online.de/pages/de/news478491

Brain Lab: the new app for simulating neurons

Gillian Queisser (BCCN Heidelberg-Mannheim, Goethe University Frankfurt), together with Michael Hoffer (Goethe University Frankfurt), developed “Brain Lab”—the first neuron simulator for iPhone and iPad that explains the basics of neuronal electrophysiology and allows to perform simple electrophysiological experiments.

Brain Lab contains two “measuring devices”: a passive integrate and fire neuron model and an implementation of the Hodgkin-Huxley model. The user can stimulate the neuron electrically and can find out how the neuronal response is influenced by changes in the Hodgkin-Huxley parameter settings.

In the near future, a number of substantial extensions are planned that will allow more complex neuronal simulations.

www.nncn.de/nachrichten-en/brainlab
Bernstein TV launched

Since February 2012, the Bernstein Network is addressing the general public also by video. Under the title “Bernstein TV”, and created by Johannes Faber (Bernstein Coordination Site) in cooperation with Gunnar Grah (Bernstein Center Freiburg), the series of videos of about 5-minutes each offers insights into current research in the Bernstein Network. Subscribe to Bernstein TV on our newly established YouTube channel:
www.youtube.com/BernsteinNetwork

Computational Neuroscience meets Visual Perception

Udo Ernst (Bernstein Awardee 2010, BGCN and University of Bremen), Cathleen Grimsen and Detlef Wegener were chosen by an international jury to organize the “European Conference on Visual Perception” (ECVP)—a renowned international conference on visual perception—in Bremen on August 25-29, 2013.

Convincing was the innovative concept to connect this already highly interdisciplinary conference with the field of Computational Neuroscience. Computational Neuroscience will be the focus topic of ECVP 2013 and will be represented in tutorials, a symposium with keynote lectures and minisymposia. Interested scientists, in particular members of the Bernstein Network, are cordially invited to submit contributions.
www.nncn.de/termine-en/ecvp2013/

Book publication: Honeybee Neurobiology and Behavior

Giovanni Galizia (left, BFNL Ephemeral Memory, BCOL Olfactory Coding and University of Konstanz), Dorothea Eisenhardt (right, BFNL Memory in Decision Making and Freie Universität Berlin) and Martin Giurfa (CNRS, Université Paul Sabatier, Toulouse) have edited the book “Honeybee Neurobiology and Behavior”. In this new publication, international experts offer a comprehensive overview over the current state of the art of neuroscientific research on the honeybee.


The Bernstein Network in social networks

In order to even better inform the national and international public about the Bernstein Network’s activities, we are now also represented in various social media. Follow us on Twitter, Facebook and LinkedIn® in order to receive all breaking news from the Bernstein Network through your favorite social network!

Follow us on Twitter:
NNCN_Germany

Find us on Facebook:
Bernstein Network Computational Neuroscience, Germany

Follow us on LinkedIn®:
Bernstein Network Computational Neuroscience, Germany
## Upcoming Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Organizers</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Jul. 5-6, 2012, Munich</strong></td>
<td>Bernstein R&amp;D Workshop Cochlear Implants</td>
<td>W. Hemmert &amp; M. Nicoletti (BCCN Munich), P. Nopp &amp; C. Wirtz (MED-EL &amp; BCCN Munich), Simone Cardoso de Oliveira (BCOS)</td>
<td><a href="http://www.nncn.de/termine-en/rudcochlearimplants">www.nncn.de/termine-en/rudcochlearimplants</a></td>
</tr>
<tr>
<td><strong>Sept. 3-7, 2012, Bochum</strong></td>
<td>Summer School: Neuronal Dynamics Approaches to Cognitive Robotics</td>
<td>E. Bicho, W. Erlhagen, G. Schöner (BFNL Learning Behavioral Models, BGCN Bochum)</td>
<td><a href="http://www.robotics-school.org">www.robotics-school.org</a></td>
</tr>
<tr>
<td><strong>Sept. 3-7, 2012, Göttingen</strong></td>
<td>10th Summer Course on Computational Neuroscience</td>
<td>D. Hofmann, A. Palmigiano, M. Puelma-Touzel (course hosted by BCCN Göttingen)</td>
<td><a href="http://www.bccn-goettingen.de/events/cns-course/cns-course">www.bccn-goettingen.de/events/cns-course/cns-course</a></td>
</tr>
</tbody>
</table>
## Upcoming Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Organizers</th>
<th>URL</th>
</tr>
</thead>
</table>
The Bernstein Network

Chairman of the Bernstein Project Committee: Andreas Herz (Munich)

The National Bernstein Network Computational Neuroscience (NCCN) is a funding initiative of the Federal Ministry of Education and Research (BMBF). Established in 2004, it has the aim of structurally interconnecting and developing German capacities in the new scientific discipline of computational neuroscience and, to date, consists of more than 200 research groups. The network is named after the German physiologist Julius Bernstein (1835–1917).

Imprint

Published by:
Coordination Site of the
National Bernstein Network Computational Neuroscience
www.nncn.de, info@bcos.uni-freiburg.de

Text, Layout:
Johannes Faber, Simone Cardoso de Oliveira, Kerstin Schwarzwälder
(News and Events)

Editorial Support:
Coordination assistants in the Bernstein Network

Design: newmediamen, Berlin

Druck / Print: Elch Graphics, Berlin

Title image: Trajectory (curved line) of a rat moving in a circular environment, together with the locations where a certain grid cell discharged (dots). © Eric Reifenstein/HU Berlin